# Health Alert

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**How to contact us:**
Office of the Director
912 Wildwood
P.O. Box 570
Jefferson City, MO 65102
Telephone: (800) 392-0272
Fax: (573) 751-6041
Website: www.dhss.state.mo.us

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION



**FROM:** **RONALD W. CATES**
**INTERIM DIRECTOR**

**SUBJECT:** **Smallpox Vaccine**

**Background**
Smallpox, caused by variola virus, is currently considered to be one of the most serious bioterrorist threats to the civilian population. This follows from the fact that smallpox is associated with high case-fatality rates (which in the past have been ≥30%), is efficiently transmitted to close contacts (household secondary attack rates are generally 50%-60%), and can result from surreptitious aerosol release of the virus by terrorists. Rapid identification of, and appropriate response to, an identified case(s) of smallpox is absolutely essential to halting additional transmission, and reducing morbidity and mortality.

Following a confirmed smallpox outbreak, rapid voluntary vaccination of a large population may be required to: 1) supplement priority surveillance and containment control strategies (i.e., ring vaccination) in areas with smallpox cases, 2) reduce the "at-risk" population for additional intentional releases of smallpox virus if the probability of such occurrences is considered significant, and 3) address heightened public or political concerns regarding access to voluntary vaccination. In addition, vaccination administered within 3-4 days post-exposure may prevent disease or severe illness caused by variola virus. In addition, development of an effective mechanism to provide rapid vaccination to large numbers of persons will prove difficult.

**Smallpox Vaccination Clinic Guide**
On September 23, 2002, the Centers for Disease Control and Prevention (CDC) announced the addition to its *Interim Smallpox Response Plan and Guidelines* of a new section titled "Smallpox Vaccination Clinic Guide." This guide describes the operational and logistical considerations associated with implementing a large-scale voluntary vaccination program in response to a confirmed smallpox outbreak. **It has been in development for several months with input from state public health officials (including representatives from Missouri) and other health care professionals, and is specifically designed to facilitate and strengthen the ability of state and local officials to quickly and effectively implement vaccination clinics in response to an outbreak of smallpox. It provides details on all aspects of immunization clinic operations and staffing, and includes an example of a model smallpox vaccination clinic.**

(continued)

It is important to note that the "Smallpox Vaccination Clinic Guide" covers post-event (i.e., after identification of a smallpox case) vaccination issues; it does not discuss pre-event issues such as which designated groups (e.g., first-responders, emergency room personnel) will be recommended to receive smallpox vaccine prior to such an event (this decision is still under review by the Federal government). Smallpox vaccine can be associated with potentially serious adverse reactions (see **Page 3-4** for a summary of some of the important clinical issues related to the vaccine).

**DHSS Position Statement**
The Missouri Department of Health and Senior Services has developed a "Position Statement on Smallpox Vaccination," which is contained on **Page 5**. It was submitted to CDC on June 8, 2002, as a statement of the department's position on issues related to the pre-event use of smallpox vaccine.

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The "Smallpox Vaccination Clinic Guide" is available at http://www.bt.cdc.gov/agent/smallpox/vaccination/pdf/smallpox-vax-clinic-guide.pdf.

The complete CDC *Interim Smallpox Response Plan and Guidelines*, which is a working document that will continue to be updated, is found at http://www.bt.cdc.gov/documentsapp/SmallPox/RPG/index.asp.

More information on smallpox is available at http://www.bt.cdc.gov/agent/smallpox/index.asp; links to specific information for medical professionals are also located at http://www.dhss.state.mo.us/BT_Response/MedicalProfessionals.htm#Smallpox.

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# Brief Summary of Smallpox Vaccine

Smallpox vaccine is a live-virus preparation of infectious vaccinia virus. Currently available only from CDC under an Investigational New Drug (IND) protocol.

The efficacy of smallpox vaccine has never been measured precisely, but studies of household contacts of a smallpox patient indicate a 91%-97% reduction in smallpox among contacts with a vaccination scar compared to contacts without a scar (these results may underestimate the actual level of protection).

Studies demonstrate that a high level of protection (nearly 100%) against smallpox persists for up to 5 years after primary vaccination and substantial but waning immunity for 10 years or more. Antibody levels after revaccination can remain high longer, conferring a greater period of immunity than occurs after primary vaccination alone.

Smallpox vaccination administered within 3-4 days of exposure to smallpox may prevent disease or severe illness caused by variola virus.

The typical clinical response to smallpox vaccination in a nonimmune person is the following:

| Symptom/Sign | Time After Vaccination |
|---|---|
| **Papule** | **3 days** |
| **Vesicle** | **5-6 days** |
| **Pustule** | **7-11 days** |
| **Maximum erythema** | **8-12 days** |
| **Scab** | **14 days** |
| **Scab separation** | **21 days** |

In addition to the vaccination site lesion, primary vaccination can produce swelling and tenderness of axillary and other regional lymph nodes, beginning 3-10 days after vaccination and persisting for 2-4 weeks after the skin lesion has healed. Fever is also common after the vaccine is administered. Approximately 70% of children experience $\geq$1 day of temperature $\geq$100ºF for 4-14 days after primary vaccination, and 15%-20% of children experience temperatures $\geq$102ºF. Fever is less common among adults.

Vaccinia virus is present at the site of vaccination beginning about 3 days after vaccination. Maximum viral shedding from the site occurs 4-14 days after vaccination, but vaccinia can be recovered from the site until the crust separates from the skin.

Complications of smallpox vaccination include:

- Inadvertent autoinoculation
  - Transfer of vaccinia from the vaccination site to another part of the body.
  - Most common sites involved are the face, eyelid, nose, mouth, genitalia, and rectum. Most lesions heal without specific treatment.
  - Most frequent complication of smallpox vaccination (accounts for ~50% of all complications); estimated to occur about once per 1,890 primary vaccination doses.

- Eczema vaccinatum
  - Localized or systemic dissemination of vaccinia virus among persons who have eczema or a history of eczema or other chronic or exfoliative skin conditions (e.g., atopic dermatitis), or among contacts of vaccinees with eczema or a history of eczema.
  - Usually mild and self-limited but can be severe or fatal.
  - Estimated to occur once per 25,000 primary vaccination doses.

- Generalized vaccinia
  - Believed to result from a vaccinia viremia with implantations in the skin in persons without eczema or other preexisting skin disease.
  - Consists of vesicles or pustules appearing on normal skin distant from the vaccination site.
  - Most rashes labeled as generalized vaccinia produce only minor illness with little residual damage.
  - Rashes diagnosed as generalized vaccinia occurs at a rate of about once per 4,000 primary vaccinations.

- Progressive vaccinia (vaccinia necrosum)
  - Severe illness with progressive necrosis in the area of vaccination, often with metastatic lesions.
  - Occurs among persons with (usually cellular) immunodeficiency.
  - Almost always fatal before the introduction of vaccinia immune globulin (VIG) and antiviral agents.
  - Occurs approximately once per 600,000 primary vaccinations.

- Postvaccinial encephalitis
  - Highest risk among children <12 months of age.
  - Presents with CNS signs, such as ataxia, confusion, paralysis, seizures, or coma.
  - Most cases are believed to result from autoimmune or allergic reactions.
  - Approximately 15%-25% of affected vaccinees die, and 25% develop permanent neurological sequelae.
  - Occurs once in about 80,000 primary vaccinations.

- Fetal vaccinia
  - Usually seen after primary vaccination of the mother in early pregnancy.
  - Usually results in stillbirth or death of the infant soon after delivery.
  - Rare (<50 cases have been reported).

- Other dermatologic conditions
  - A variety of erythematous or urticarial rashes can occur approximately 10 days after primary vaccination. The rash usually resolves spontaneously within 2-4 days.
  - Rarely, bullous erythema multiforme (Stevens-Johnson syndrome) occurs.

- Death
  - Death resulting from smallpox vaccination is rare, with past estimates being approximately 1 death per million primary vaccinations and 1 death per 4 million revaccinations. However, given the larger numbers of immunocompromised persons in our society today, the actual death rate could be slightly higher.
  - Most often the result of postvaccinial encephalitis or progressive vaccinia.

Sources: 1) CDC. *Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)* (7th Ed.); April 2002.
2) CDC. *Interim Smallpox Response Plan and Guidelines*.

**MISSOURI DEPARTMENT OF HEALTH AND SENIOR SERVICES (DHSS)**
**CURRENT POSITION STATEMENT ON SMALLPOX VACCINATION**
**June 8, 2002**

**Background**

a) Effectiveness of the CDC-recommended ring vaccination approach, as part of a search and containment strategy, under a bioterrorism (BT) scenario is not yet clear. Although there is scientific evidence with the success of this strategy for naturally occurring outbreaks, little is known about the intentional introduction of multiple foci of smallpox, possibly at different times. Control measures may differ under a BT scenario;
b) Smallpox vaccination is effective even if given four days after first exposure to smallpox. There is thought to be a 50 percent benefit if vaccinated up to 7 days after exposure. There is no more than a 20 percent benefit if vaccinated more than one week after exposure. (Fenner F Henderson DA, et al. WHO Geneva "Smallpox and its Eradication," 1988, page 65.);
c) There is a large population susceptible to smallpox with many people at risk for vaccine complications. The risk of complications was estimated thirty years ago at 1,254 per million for primary vaccination and 108 per million for re-vaccination. (Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccination, 1968. National Surveillance in the United States. N Engl J Med 281:1201-1208; 1969) The number of complications will likely be higher today due to the higher number of chronically immunosuppressed patients than thirty years ago (e.g., those living with cancer, HIV positive and AIDS patients);
d) The U.S. Department of Health and Human Services is under considerable pressure to make the smallpox vaccine available even before clinical trials are completed and FDA approval is obtained. There is little evidence to support making the vaccine available to the general public because the "scientific model" for cost-effectiveness (or cost-benefit) lacks crucial information on the level of risk of acquiring smallpox (that is, the risk of an attack). Information is available only for vaccine efficacy and the risk of complication. Without a quantifiable estimate of the risk for acquiring smallpox at this time, cost-effectiveness (or cost-benefit) models cannot be validly construed.

**Recommendations**

We recommend as initial strategy that a small, limited stockpile (cache) be maintained by the Missouri Department of Health and Senior Services to support immediate prevention and control measures at the local level, mainly targeted at persons most at risk for exposure in a smallpox event, which would include emergency room staff, emergency medical technicians and public health workers. We also support the ring vaccination strategy that CDC recommends and use of epidemiological data to assess initial strategy and guide future prevention and control measures.

Specifically, prevention and control measures would consist of a combination of:

- Use of small state stockpile for limited **pre-event** vaccination on a voluntary basis for pre-identified and eligible (i.e., screened for contra-indication) first responders involved in state and local health response teams or level C containment facilities identified through statewide bioterrorism planning;
- Use of small state stockpile for immediate vaccination, on a voluntary basis, after occurrence of a smallpox case (**after-event**) for the same group of pre-identified responders who have not been vaccinated and will likely be exposed to smallpox;
- Use of remaining state stockpile and federal stockpile for supporting prevention and control measures **after-event** with **ring vaccination**, on a voluntary basis, to be implemented jointly with active surveillance, case identification and containment of cases and contacts.

Note: **Pre-event** means use of the vaccine before index case is identified. **After-event** means use of vaccine after index case is identified. The **surveillance and containment strategy** relies on prompt identification of cases and their isolation; identification and vaccination of contacts of cases (household members and face-to-face contacts); vaccination of contacts of first ring contacts; and the judicious use of vaccine supply. **Ring vaccination** involves the vaccination of contacts and contacts of contacts in a circular ring.